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☐ 1: Neuroscience. 1995 Jan;64(2):385-95.

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Alteration in nicotine binding sites in Parkinson's disease, Lewy body dementia and Alzheimer's disease: possible index of early neuropathology.

Perry EK, Morris CM, Court JA, Cheng A, Fairbairn AF, McKeith IG, Irving D, Brown A, Perry RH.

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High-affinity nicotine binding, considered to primarily reflect the presence of CNS alpha 4 beta 2 nicotinic receptor subunits, was examined autoradiographically in brain regions most severely affected by Alzheimer and Parkinson types of pathology. In the midbrain, the high density of binding associated with the pars compacta of the substantia nigra was extensively reduced (65-75%, particularly in the lateral portion) in both Lewy body dementia and Parkinson's disease. Since loss of dopaminergic neurons in Lewy body dementia was only moderate (40%), loss or down-regulation of the nicotinic receptor may precede degeneration of dopaminergic neurons in this region. In the dorsolateral tegmentum, where diffuse cholinergic perikarya are located, nicotine binding was highly significantly decreased in both Lewy body dementia and Parkinson's disease with almost no overlap between the normal and disease groups, indicative of a major pathological involvement in or around the pedunculopontine cholinergic neurons. In the hippocampus, binding was decreased around the granular layer in Lewy body dementia and Alzheimer's disease, although unchanged in the stratum lacunosum moleculare, where binding was relatively higher. Dense bands of receptor binding in the presubiculum and parahippocampal gyrus--areas of highest binding in human cortex--were diminished in Alzheimer's disease but not Lewy body dementia. In temporal neocortex there were reductions in Alzheimer's disease throughout the cortical layers but in Lewy body dementia only in lower layers, in which Lewy bodies are concentrated. Abnormalities of the nicotinic receptor in the diseases examined appear to be closely associated with primary histopathological changes: dopaminergic cell loss in Parkinson's disease and Lewy body dementia, amyloid plaques and tangles in subicular and entorhinal areas in Alzheimer's disease. Loss or down-regulation of the receptor may precede neurodegeneration.

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